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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,911	05/11/2007	Steven A. Boyd	AV 35	6038

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EXAMINER	
MCDOWELL, BRIAN E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
03/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,911	BOYD ET AL.	
	Examiner	Art Unit	
	BRIAN MCDOWELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/15/2008 X 2*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

/BEM/

DETAILED ACTION

RESPONSE TO ELECTION/RESTRICTION

Applicant's election with traverse of group I and elected specie in the reply filed on 1/8/2010 is acknowledged. The traversal is on the ground(s) that the inventions as claimed are related and have a common utility. This is not found persuasive because the inventions were found to lack a special technical feature as described in the previous office action.

Furthermore, the claimed inventions encompass different subject matter and would require multiple structure search queries. Thus, the examiner would encounter a *serious* search burden if a restriction requirement was not implemented. The requirement is still deemed proper and is therefore made FINAL.

An action on the merits of claims 1, 2, 4-11, and 23-25 is contained herein.

Priority

This application receives the priority date of 3/24/2004, drawn to provisional application 60/556,218.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-11, and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In all occurrences wherein "derivative" is cited, the claims are rendered indefinite for the following reason:

In the absence of the specific derivatizations to the claimed pyridinyl compounds or distinct language to describe the structural modifications or the chemical names of derivatized compounds of this invention, the identity of said derivatives would be difficult to describe and the metes and bounds of said derivatives applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims. The examiner recommends that "derivative" is removed from the claims.

Claim 1 cites a "tumor-targeting moiety". What are the chemical structures of these moieties? The specification only exemplifies a few examples that vary drastically in chemical structure (e.g., peptides and carbohydrates). Does this limitation include other moieties other than peptides or carbohydrates? (e.g., complex proteins, lipids, or other drugs). The examiner recommends that this term is removed from the claims.

Claim 8 cites R^7 or R^9 may be an "antibody" (also see claim 9). The examiner can not readily interpret the metes and bounds of this limitation. What are the structures of the claimed "antibodies" of the invention. The examiner recommends that this term is removed from the claims.

Claim 4 cites that R^3 is "-$NR^0C(O)R$". There is insufficient antecedent basis for this limitation in the claim.

Claim 8 cites that R^7 or R^9 may be "-$[C(O)CH(R)N(R)]_{2-3}$-R". There is insufficient antecedent basis for this limitation in the claim.

Claim 10 is rejected under 35 U.S.C. 112, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim.

In the instance of claim 10, applicant is claiming a group of compounds which are embedded in tables 1-2 of the instant specification, which does not comply with 35 U.S.C. 112 *2nd*. See *Ex parte Fressola*, 27 USPQ2d 1608:

"The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention. Claims in utility applications [1] that define the invention entirely by reference to the specification and/or drawings, so-called "omnibus" or "formal" claims, while perhaps once accepted in American patent practice, are properly rejected under Section 112 Para. 2 as failing to particularly point out and distinctly claim the invention. See MPEP Section 706.03(h) (5th ed., rev. 14, Nov. 1992); Landis, Mechanics of Patent Claim Drafting, Section 2 (1974). This analysis is limited to claims in utility applications. Plant patent claims are defined "in formal terms to the plant shown and described." Claims in design patents are recited in formal terms to the ornamental design "as shown" or, where there is a properly included special description of the design, the ornamental design "as shown and described." MPEP Section 1503.01…….The general rule is that the claims should be self-contained; that is, they should not expressly rely upon the description or drawing to give them meaning. . . . The terms "substantially as described" and the like, once much used in claims (GLASCOCK 1943 Section 5640) are now rarely seen. The Office disregards them in interpreting claims. . . . Claims consisting only in a reference to the disclosure, as "The features of novelty herein disclosed," are not allowed except in design cases……A claim which refers to the specification defeats the purpose of a claim."

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-9, and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds and/or compositions wherein R^6 is not "M", does not reasonably provide enablement for the other thousands of compounds that applicant is claiming. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444. Analysis is described below:

(A) Breadth of claims: The formula I is drawn to a myriad of substituents that vary independently and lead to compounds of a wide variety of structures. These compounds encompass molecules that widely vary in the physical and chemical properties such as size, molecular weight, acidity, basicity, and properties that are known in the art to greatly influence pharmacokinetic and pharmacodynamic parameters, not to mention the ability to productively bind to

claimed biological target molecules. The claims cover compounds easily in the millions given the number of possible rings, ring systems covered by the claims' scope along with varying choices for remaining variables; thus the claims are very broad.

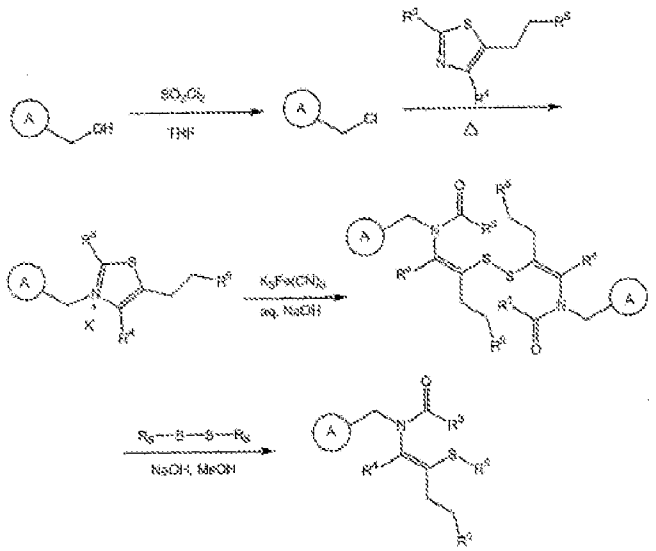
(B) The nature of the invention: The invention is closely related to the field of medicinal chemistry. More specifically, utilizing thioalkeneamides of the formula I as transketolase inhibitors to treat cancer and other associated diseases.

(C), (E) State of the Prior Art: Chemistry is unpredictable. See *In Re Marzocchi* and Horton 169 USPQ at 367 paragraph 3:

"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task.

In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)" Dorwald F. A. Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

Take for example the following synthetic scheme which introduces the disulfide bond functionality of the instantly claimed compounds (see page 22):



The last synthetic step entails cleavage of the disulfide bond with a disulfide reagent affording the final compound. However, applicant's claims are drawn to compounds wherein R^6 are various metals (e.g., Li, Na, K, etc.), affording organometallic compounds which can not be obtained by employing the synthetic scheme above. The resulting compounds are not readily recognized in the art and would contain metals which are lacking covalent bonds (e.g, R-S-Mg, etc.). Furthermore, there is no direction within the instant specification that would guide one of ordinary skill as to how to prepare and use these organometallic reagents as therapeutic agents.

(D) Skill of those in the art: The level of skill in the art is high and one would require a Ph.D. in the field of synthetic organic chemistry.

(F) Direction or Guidance: Little guidance or direction is provided by applicant in reference to making compounds wherein R^6 are various metals (e.g., Li, Na, K,

etc.). Specification offers no teachings or suggestion as to how to make and use these compounds. Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.";

(G) Working Examples: The compound core depicted with specific substituents represent a narrow subgenus for which applicant has provided sufficient guidance to make and use; however, this disclosure is not sufficient to allow extrapolation of the limited examples to enable the scope of the compounds instantly claimed.

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP 608.01(p).

(H) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome. Applicant fails to provide guidance and supporting information for how to make and/or use compounds wherein R^6 are metals, therefore undue experimentation would be expected.

Due to the level of unpredictability in the art, the very limited guidance provided, and the lack of working examples, the applicant has shown lack of enablement. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRIAN MCDOWELL whose telephone number is (571)270-5755. The examiner can normally be reached on Monday-Thursday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/B.E.M./
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